

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1. (Original) A nucleic acid encoding a Diphtheria toxin fusion protein comprising
  - (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator; and
  - (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically binds to a protein overexpressed on the surface of a cell.
2. (Original) The nucleic acid of claim 1, wherein the matrix metalloproteinase is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and membrane-type1 MMP (MT1-MMP).
3. (Original) The nucleic acid of claim 1, wherein the plasminogen activator is selected from the group consisting of tissue plasminogen activator (t-PA) and urokinase plasminogen activator (u-PA).
4. (Previously Presented) The nucleic acid of claim 1, wherein the matrix metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ (SEQ ID NO: 20).
5. (Currently Amended) The nucleic acid of claim 1, wherein the plasminogen activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID NO: 23), GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).
6. (Original) The nucleic acid of claim 1, wherein the protein overexpressed on the surface of a cell is a receptor.

1                   7.       (Original) The nucleic acid of claim 1, wherein the heterologous  
2 polypeptide comprises a cytokine.

1                   8.       (Original) The nucleic acid of claim 1, wherein the heterologous  
2 polypeptide comprises a growth factor.

1                   9.       (Original) The nucleic acid of claim 1, wherein the heterologous  
2 polypeptide is a member selected from the group consisting of: IL-2, GM-CSF, and EGF.

1                   10.      (Original) The nucleic acid of claim 1, comprising the nucleotide  
2 sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13.

1                   11.      (Original) A vector comprising the nucleic acid of claim 1.

1                   12.      (Original) The nucleic acid of claim 6, wherein the cell is a cancer cell.

1                   13.      (Original) The nucleic acid of claim 7, wherein the heterologous  
2 polypeptide comprises GM-CSF.

1                   14.      (Original) The nucleic acid of claim 7, wherein the heterologous  
2 polypeptide comprises IL-2.

1                   15.      (Original) The nucleic acid of claim 8, wherein the heterologous  
2 polypeptide comprises EGF.

1                   16.      (Original) A nucleic acid encoding a Diphtheria toxin fusion protein  
2 comprising

3                   (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
4 been substituted for a cleavage site for a urokinase a plasminogen activator; and

5                   (2) GM-CSF.

1                   17.      (Original) A polypeptide encoded by the nucleic acid of claim 1.

1                    18.    (Original) A polypeptide encoded by the nucleic acid of claim 10.

1                    19.    (Original) A polypeptide encoded by the nucleic acid of claim 16.

1                    20.    (Original) A host cell comprising the vector of claim 11.

1                    21.    (Original) The nucleic acid of claim 12, wherein the cancer is leukemia.

1                    22.    (Original) The nucleic acid of claim 12, wherein the cancer is acute  
2 myelogenous leukemia.

1                    23.    (Original) A pharmaceutical composition comprising the protein of claim  
2 18 and a pharmaceutically acceptable carrier.

1                    24.    (Original) A method of treating cancer, the method comprising  
2 administering to a subject a Diphtheria toxin fusion protein comprising  
3 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
4 been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator;  
5 and  
6 (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically  
7 binds to a protein overexpressed on the surface of a cell.

1                    25.    (Original) The method of claim 24, wherein the matrix metalloproteinase  
2 is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and  
3 membrane-type1 MMP (MT1-MMP).

1                    26.    (Original) The method of claim 24, wherein the plasminogen activator is  
2 selected from the group consisting of t-PA and u-PA.

1                    27.    (Previously Presented) The method of claim 24, wherein the matrix  
2 metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ (SEQ ID  
3 NO: 20).

1                   28.     (Previously Presented) The method of claim 24, wherein the plasminogen  
2 activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID NO: 23),  
3 GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).

1                   29.     (Original) The method of claim 24, wherein the protein overexpressed on  
2 the surface of a cell is a receptor.

1                   30.     (Original) The method of claim 24, wherein the cell is a cancer cell.

1                   31.     (Original) The method of claim 24, wherein the heterologous polypeptide  
2 comprises a cytokine.

1                   32.     (Original) The method of claim 24, wherein the heterologous polypeptide  
2 comprises a growth factor.

1                   33.     (Original) The method of claim 24, wherein the fusion protein is encoded  
2 by the nucleotide sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13.

1                   34.     (Original) The method of claim 30, wherein the cancer is leukemia.

1                   35.     (Original) The method of claim 30, wherein the cancer is acute  
2 myelogenous leukemia.

1                   36.     (Original) The method of claim 31, wherein the heterologous polypeptide  
2 comprises GM-CSF.

1                   37.     (Original) The method of claim 31, wherein the heterologous polypeptide  
2 comprises IL-2.

1                   38.     (Original) The method of claim 32, wherein the heterologous polypeptide  
2 comprises EGF.

1                   39.     (Original) The method of claim 24, wherein the Diphtheria toxin fusion  
2 protein comprises:

3                   (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
4 been substituted for a cleavage site for a urokinase plasminogen activator; and

5                   (2) GM-CSF.

1                   40.     (Original) A method of targeting a compound to a cell overexpressing a  
2 cytokine receptor or a growth factor receptor, the method comprising the steps of:

3                   administering to the cell Diphtheria toxin fusion protein comprising

4                   (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
5 been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator and  
6 wherein the Diphtheria toxin is cleaved by a matrix metalloproteinase or a plasminogen  
7 activator; and

8                   (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically  
9 binds to a cytokine receptor or a growth factor receptor.

1                   41.     (Original) The method of claim 40, wherein the cell also overexpresses a  
2 matrix metalloproteinase, a tissue plasminogen activator, or a urokinase plasminogen activator.

1                   42.     (Original) The method of claim 40, wherein the matrix metalloproteinase  
2 is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and  
3 membrane-type1 MMP (MT1-MMP).

1                   43.     (Original) The method of claim 40, wherein the plasminogen activator is  
2 selected from the group consisting of t-PA and u-PA.

1                   44.     (Previously Presented) The method of claim 40, wherein the matrix  
2 metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ SEQ ID  
3 NO: 20).

1                   45.     (Previously Presented) The method of claim 40, wherein the plasminogen  
2 activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID NO: 23),  
3 GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).

1                   46.     (Original) The method of claim 40, wherein the cancer cell is a leukemia  
2 cell.

1                   47.     (Original) The method of claim 40, wherein the cancer cell is an acute  
2 myelogenous leukemia cell.

1                   48.     (Original) The method of claim 40, wherein the Diphtheria toxin fusion  
2 protein comprises  
3                   (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has  
4 been substituted for a cleavage site for a urokinase plasminogen activator; and  
5                   (2) GM-CSF.

1                   49.     (Original) An isolated nucleic acid comprising the sequence set forth in  
2 any one of SEQ ID NOS: 2-18.